APPROVED O.G. FIG.

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Docket No.: 2719.2001-000

Synthesis of Oligonucleotide Array

Inventor: Glenn H. McGall

#### Figure 1A

Px = phosphoramidite, H-phosphonate or phosphate

Y = one of the general structures in Figures 1B-1I ( $R_1$  = -H, alkyl or aryl):

#### Figure 1B

o-nitrobenzylthioethyloxycarbonyl (NBTEOC)

Figure 1C

o-nitrophenylaminocarbonyl (NPAC)

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ynthesis of Oligonucleotide Arrays..

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# Figure 1D

o-nitrophenoxycarbonyl (N2POC)

Figure 1E

m-nitrophenoxycarbonyl (N3POC)

Figure 1F

o-nitrophenylthioethyloxycarbonyl

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Inventor: Glenn H. McGall



# Figure 1G

 $\alpha$ -methyl-8-nitronaphthylmethoxycarbonyl (MeNMOC)

#### Figure 1H

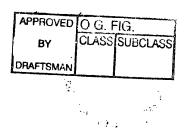
6-substituted 2-(o-nitrophenyl)-2-propyloxycarbonyl (6NPPOC)

A = O, S, N-alkyl, N-aryl,  $(CH_2)_n$ , where n = 0 to about 3 B = aprotic weakly basic group (e.g., N-alkylimidazole)

#### Figure 1I

cyclic o-nitrobenzyloxycarbonyl

A = O, S, N-alkyl, N-aryl,  $(CH_2)_n$ , where n = 0 to about 3 B = aprotic weakly basic group (e.g., N-alkylimidazole)



To Synthesis of Oligonucleotide Arrays Inventor: Glenn H. McGall



TEMPOC

NAMOC

NP2POC

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Inventor: Glenn H. McGall



# Figure 2B Coupling Efficiency Data

Y}	Stepwise yield	photolysis conditions
(MeNPOC-control)	about 88 %	nonpolar solvent
NO <sub>2</sub> CH <sub>3</sub>	about 85 %	МеОН
NO <sub>2</sub>	95 %	DMSO
Me NO2	94 %	Nucleophilic solvent (MeOH)
MeO NO <sub>2</sub>	about 80 %	Nucleophilic solvent (MeOH)
MeQ O O O O O O O O O O O O O O O O O O O	about 75 %	Nucleophilic solvent (MeOH)
NO <sub>2</sub> CH <sub>3</sub>	90 %	basic solvent (1 % NMI/DMSO)
Me O O	96 %	DMSO

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Docket No.. 2719.2001-000 Synthesis of Oligonucleotide Arrays Inventor: Glenn H. McGall

# Figure 3

# 5'-TEMPOC-T-Phosphoramidite

- Dyer, et al. JOC 64: 7988 (1999)
   Tetrahedron Lett., 38(52), 8933-4 (1997)
   McGall, et al. JACS 119: 5081 (1997)
   Triphosgene may work equally well for this step.
   Chloroformate can probably be used without purious.
- 5. Chloroformate can probably be used without purification.

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Docket No.: 2719.2001-000

Synthesis of Oligonucleotide Arrays

Inventor: Glenn H. McGall

# Figure 4

# Synthesis of NINOC-T-CEP

R = H, alkyl, alkoxy

- 1. Bromridge, et al. (1998) J. Med. Chem. 41: 1598.
- 2. (i) Brooker, L.S., et al. (1953) US Pat. 2,646,430; (ii) Boekelheide, et at. (1954) J. Org. Chem. 19: 504.; (iii) Bennet, et al (1941) J. Chem Soc. 74: 244.
- 3. Mortensen, et al. (1996) Org. Prep. Proc. Int. 28: 123.

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Titl ynthesis of Oligonucleotide Arrays.

Inventor: Glenn H. McGall

Figure 5

# Me2NPOC-T-CEP

$$\frac{(iPr_2N)_2POCE}{(iPr_2N)_2NH/}$$
 tetrazole 
$$\frac{NC}{NC} = \frac{N}{NiPr_2}$$

	1	
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Synthesis of Oligonucleotide Array

Inventor: Glenn H. McGall

# Figure 6

#### Me3NPOC-T-CEP

$$\frac{(iPr_2N)_2POCE}{(iPr_2N)_2NH/}$$

$$tetrazole$$

$$NH$$

$$OMe$$

$$O$$

$$O$$

$$NNPr_2$$

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Synthesis of Oligonucleotide Arra
Inventor: Glenn H. McGall

# Figure 7

#### NP2POC-T-CEP

$$\frac{(iPr_2N)_2POCE}{(iPr_2N)_2NH/}$$
tetrazole
$$NC$$

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Synthesis of Oligonucleotide Array Inventor: Glenn H. McGall

# Figure 8

#### **NNEOC-T-CEP**